**Endemic Equine Neurological Diseases**
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The main differentials for infectious neurological disease include **rabies, equine herpesvirus 1 (EHV-1), equine protozoal myeloencephalitis, verminous encephalitis, liver disease and creeping indigo.** There are multiple viruses that cause encephalitis in the horse and are transmitted by mosquitoes and the main include: **Eastern Equine Encephalitis (EEE) virus, Western Equine Encephalitis (WEE) virus, and West Nile virus (WNV.) Horses in florida are always at riske for Venezuelan equine encephalitis.**

**EPM**

Until West Nile Virus encroachment, equine protozoal myeloencephalitis (EPM) was considered the most common cause of infectious neurologic disease in horses in the United States. Many horses likely encounter myelitis-causing protozoal organisms, ***Sarcocystis neurona*** or ***Neospora hughesi,*** at some point in their life without developing detectable neurologic disease (asymptomatic infection). However little is known about why one horse gets EPM and the other does not. Our inability to cause disease after giving horses cysts collected from opossums prevents us from testing treatments *and vaccines*. Without a basic understanding of how this disease progresses from an asymptomatic, infected animal to one with neurologic disease, little further work can be performed investigating how to diagnose, control, or prevent infection. S. neurona is an Apicomplexa and has a complex life-cycle where a definitive host serves as a predator and the intermediate host is prey. The intermediate host of *S. neurona* consists of cats, armadillos, skunk, raccoons and sear otters. However the horse is considered an aberrant host. Only the opossum has been demonstrated to be a definitive host thus far. Even less is understood is the Neosporosis life-cycle in horses. The horse is likely an aberrant host with the definitive horses likely a canid species and a herbivore serving as the intermediate host.

**Clinical Signs:** Clinical signs in affected horses vary from mild muscle wasting or vague lameness to recumbency, convulsions, and death. The variability of clinical signs due to *S. neurona* makes clinical identification without ancillary testing at times difficult. Although onset may be slow and insidious, many horses develop acute neurological dysfunction. Cranial nerve involvement reflects its predilection for the hindbrain in horses. Inability to walk can be present and can symmetrical or asymmetrical. Weakness and muscle atrophy in one or more limbs is common. Muscle atrophy is also associated with cranial nerve dysfunction and most often occurs with side of the check will waste away causing horses to have difficulty eating.

**Relapsing EPM-What causes this?**
Who knows, but I suspect that horses that initially develop clinical signs become re-exposed and develop disease again. In other words, what determines susceptibility in that horse probably determines life long susceptibility to the disease overall. Others theorize that treatment of infection does not result in a sterile response. *S. neurona* does not form cysts in the brain and spinal cord, so long-standing infection has not really been characterized. Other Apicomplexa are noted for lack of long term immunity so neither of these theories are far fetched. Anecdotal

relapse rates on folic acid inhibitors vary between 30 and 50%, while anecdotal reports on triaxines are less than 10%. However, relapses do occur on both classes of drugs, so long term intermittent therapy is suggested should one have a patient that tends to relapse.

## Viral Encephalitides

### Rabies

Rabies (lyssavirus) reservoirs in bats and skunks and most rabies affecting horses are consistent with the bat strain. Although rabies is rare in horses (compared to other forms of infectious neurological disease), horses are susceptible to fulminate rabies and due serve as a public health risk if diseased. Thus identification of potential rabies suspects is essential. Risk factors associated with rabies are fairly obvious such as contact with enzootic species, pasture management, recent travel to areas of high activity.

**Clinical Signs:** Rabies is primarily transmitted by oral inoculation in the horse. After initial viral replication at the site of infection, transaxonal movement from peripheral nerves to the CNS occurs. Saliva and other body tissues become virus positive at the time of clinical signs. Rabies is one of the most variable neurologic diseases in the horse. Insidious onset is the hallmark of initial clinical signs and reports consist of lameness, colic, dysuria, priapism in addition to neurological disease. Primary clinical signs include anorexia, fever, depression, blindness, mania, dysphasia, hyperesthesia, muscle-twitching, lameness, paralysis, incontinence, and sudden death. Neurological manifestations have been known to emphasize either brain or spinal cord disease. With the paralytic form, horses experience ascending paralysis and hyperesthesia is common and is manifest by self-mutilation. Behavioral changes occur as in other species with horses presenting as dumb or furious. In the latter horse are maniacal and extremely dangerous.

**Prevention:** Since there is no means of rabies therapy, prevention is the key. Rabies prophylaxis should be administered to horses on an annual basis after the initial series. In foals vaccination should commence at 3-4 months of age (following primary series recommendations). Housing of wild animals as pets is discouraged and surveillance of abnormally acting wildlife is important. Immunoprophylaxis of all domestic carnivores is a must.

### Arboviruses

**Lifecycle of Arboviruses**

***Arboviruses*** are transmitted primarily by mosquitoes. Usually there is an animal or avian host in which the virus multiplies high enough so that mosquitoes become infected with virus while feeding. Multiple species may seroconvert or possibly become clinical, however only those develop significant are reservoir hoses. For both the alphaviruses, EEE and WEE, and the flaviviruses, non-mammalian hosts such as birds appear to develop a high enough titer of virus in the blood to transmit the virus back to mosquitoes.

Equine Eastern Encephalitis (EEE) virus is an alphavirus and has caused encephalitis in U.S. horses since its first known isolation in 1938. The focus of this disease is usually the East coast with cases occurring as far West as Ohio. The mosquito vector for EEE includes members of the *Aedes* sp. and *Coquillettidia perturbans*.

Western equine encephalitis affects horses less severely than EEE. Like its name, its primary focus is the Midwest and West. There is a form with yearly activity in Florida that is known as Highland's J virus. There have been around 600 cases in humans since isolation of WEE in California in 1930. There have been notably large equine outbreaks over the years; for instance the Utah epizootic in 1933 affected almost 4,000 horses. The most important vector of this disease is *Culex tarsalis*.

Venezuelan equine encephalitis has a fairly restricted geographical distribution to Central and South America although U.S. incursions have occurred. The most notable incursion was during the early 1970's. Several efficient vectors have been identified and these include common genera, *Aedes*, *Anopheles* and *Culex* spp.

West Nile virus is a flavivirus and was recently introduced to the United States in 1999 and causes neurological disease in birds, horses, and humans. The primary mosquito vector for the U.S. outbreak is *Culex pipiens*, however many other species of mosquitoes have contributed to this epidemic. The exact vector(s) for horse disease is still unknown. Experimental infection using *Aedes albopictus* mosquitoes has resulted in seroconversion and subclinical infection. In both EEE, WEE and WNV virus, birds only appear to develop a significant level of virus in their blood and can thus transmit the respective disease. *An infected WNV or EEE horse is not infections and poses no risk to other horses, humans, or birds.* With VEE, horses do develop a high enough viral titer to transmit to mosquitoes, therefore, horses have a reservoir role in VEE infections. In fact, during epizootics, horses are important amplifiers of the virus.

During of summer of 2003, an EEE outbreak occurred in the Southeast. While EEE cases in the southeast averages 5-30 per state with Florida usually having the most reported cases usually between 20 and 40 per year. This last year, the state of Florida had 186 affected horses alone. North Carolina also had exceptionally high activity with 80 cases. Since 1999, over 16,000 U.S. horses have been confirmed for WNV encephalomyelitis. During 2002, 14,717 horses were affected with a 30% mortality rate.

## Herpesvirus Myeloencephalitis

Herpesvirus myeloencephalitis is caused by an alphavirus that cause neurologic signs due to development of vasculitis, thrombosis, and necrosis of neurological tissue. The virus infects the vascular endothelium of the blood-brain barrier and causes widespread vascular injury. This vascular injury then causes secondary neuronal damage. Herpesvirus myeloencephalitis occurs as clusters and may be associated with a previous respiratory outbreak.

The Herpesvirus most associated with neurological manifestation is a type 1 virus (EHV-1) that has a short incubation, reproductive cycle and has the ability to form latent infection. It is presently hypothesized that the specific strain of EHV-1 most associated with neurogical Herpesvirus has only one nucleotide change.

**Clinical Signs.** Like most infectious neurological diseases, the clinical signs and course of therapy is variable. Primarily this virus causes a symmetrical ataxia and weakness of the pelvic

limbs with urinary incontinence, loss of sensation and motor deficits around the tail and perineal area. Gait deficits can be initial minor, resemble lameness and then rapidly progress to recumbence.

**Criteria for Herpesvirus -1 diagnosis and Biosafety Precautions**

The combination or history of URI in a herd, clinical disease consistent with EHV-1 myeloencephalopathy, virus isolation from pharyngeal or nasal secretions or buffy coat will provide a strongly presumptive diagnosis of EHV-1. Biosafety procedures should be instituted at this time: restriction of new horses into the group, minimize stress in exposed horses, restriction of movement out of the herd for 21 days at least is recommended Most of the viral shedding takes place during the initial respiratory phase however, many neurological horses are still shedding virus.

## VERMINOUS ENCEPHALITIS

Verminous encephalitis is rare but does occur in the Midwest and Southeast. Causes to consider specifically in Florida include Strongylus vulgaris, Setaria filariids, Halicephalobus gingivalis, and Drachia megastoma, and Hypoderma. Setaria and Strongylus cause brain or spinal cord disease. Signs are ipsilateral and sudden, due to an infarctive process. Halicephalobus and Hypoderma usually are intracranial.
Hemorrhage and high numbers of eosinophil and neutrophils occur with verminous CNS disease. There is marked discoloration of the CSF.
Verminous infections are usually composed of elevated eosinophil counts with high gamma globulins peripherally.

## Summary of Endemic Infectious Neurological Diseases

Infectious CNS diseases that share clinical signs of encephalitis include rabies, equine protozoal myeloencephalitis (EPM), equine herpes virus-1 (EHV-1), less likely botulism, and verminous meningoencephalomyelitis (*Halicephalobus gingivalis*, Setaria, *Strongylus vulgarus*). Non-infectious causes to consider include hypocalcemia, toxicities, and liver disease from crotolaria. With rabies, signs of cerebral involvement are common. Change in consciousness is characterized by behavioral alterations, depression, seizure, and coma. Motor function is abnormal, characterized by circling, propulsive walking, or head pressing. Cortical blindness can also be present. Cranial nerve signs are also common including pharyngeal/laryngeal dysfunction, and paresis of the tongue. Head tilt is not common. Differentiation from rabies can be quite problematic if signs include ataxia, weakness, or gait abnormalities. Alphaviruses, rabies, *H. gingivalis* infection, hepatoencephalopathy, and leukoencephalomalacia are usually progressive with cortical signs. Spinal disease due to EPM is a more difficult differential if horses with WNV are not febrile and do not exhibit excessive muscle fasciculations. Although WNV infection throughout the spinal cord is fairly symmetrical, horses can present with asymmetrical and/or multifocal cranial nerve and gait deficits. Equine herpesvirus myeloencephalopathy is a white matter infection in which clinical signs vary from subtle gait deficits to profound hind limb weakness, ataxia, and paraplegia. Urinary incontinence, tail elevation, and anal and tail hypotonia are common.